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09/868,195	09/14/2001	Martin John Glenton Hughes	GJE-71	7256

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 01/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,195	HUGHES ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on 12-25-04

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 25,27,28 and 32-46 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 25,27,28 and 32-46 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment and declaration filed 10-25-04 have been entered into the record. Claims 25, 27, 28, 32-46 are pending and under examination. Claims 1-24, 26 and 29-31 have been cancelled.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Applicant's remarks are noted with respect to the priority documents and the objection is withdrawn.

Rejections Withdrawn

The rejection of claims 25-29 under 35 U.S.C. 102(b) as being clearly anticipated by Itoh et al, (Microbiology and Immunology, 30(4):297-306, 1986) is withdrawn in view of Applicants amendments to the claims.

The rejection of claims 25-29 under 35 U.S.C. 102(b) as anticipated by Ichiman et al (Canadian Journal of Microbiology 28(7):726-732, 1982) is withdrawn in view of Applicants amendments to the claims.

The rejection of claims 25-28 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is as lacking written description is withdrawn in view of the amendment to insert new matter as set forth below.

Rejections Maintained

Claims 25-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained for reasons made of record for claims 25-29 in the Office Action mailed 4-21-04.

Applicants' arguments and the Declaration of Dr Moore have been carefully considered but are not persuasive. The claims are drawn to methods of treatment or prevention of a Group B Streptococcal infection comprising administering to a patient in need of such an immunogenically effective amount of an isolated bacterial NADP-dependent glyceraldehyde-3-phosphate dehydrogenase, wherein the NADP-Dependent Glyceraldehyde -3-Phosphate Dehydrogenase is obtainable from Group B streptococcus, *Streptococcus mutans*, a polypeptide as set forth in SEQ ID NO:12 or any immunological fragment thereof. In these claims, it is specifically the animal that is injected must be protected or treated. Turning to the declaration, the declaration provides incomplete characterization, methodology and results to support enablement of *the claimed invention.*

With respect to the declaration, Declarant indicates that the present invention is based on the finding that the protein NADP-Dependent Glyceraldehyde -3-Phosphate Dehydrogenase is a surprisingly good candidate for use as a vaccine against a Group B Streptococcal infection. This is not persuasive, the specification does not set forth NADP-Dependent Glyceraldehyde -3-Phosphate Dehydrogenases from bacteria in general, nor does the declaration present evidence that any bacterial NADP-dependent glyceraldehyde-3-phosphate dehydrogenase can protect against infection or prevent infection. Declarant describes MS10 as a NADP-Dependent Glyceraldehyde -3-Phosphate Dehydrogenase. The specification does not support this assertion. The specification teaches that homologs of MS10 are the subgenus of Nonphosphorylating, NADP-Dependent Glyceraldehyde -3-Phosphate Dehydrogenase and Declarant does not explain this discrepancy. Declarant acknowledges that the MS10 polypeptide of the specification was identified as a putative vaccine candidate and by filing of the declaration admits that testing was necessary to determine its ability to provide for a protective effect upon administration (see paragraph 3 of the declaration). The courts have held that the disclosure is insufficient when testing is necessary to determine the actual use or possible lack of use *(In re Kirk and Petrow* (CCPA) 153 USPQ 48). The declaration indicates that a

vaccine composition of "MS10" was injected into rabbits. "MS10" is described in the specification as "obtainable from Group B Streptococcus" and therefore it is not clear from the declaration what the specific structure of the protein or the composition comprising the protein that was injected into rabbits. There is no clear correlation between any particular protein structure and composition injected and "MS10" for reasons made of record in the written description requirement of the last office action and the now claimed invention. Declarant appears to redefine all MS10 polypeptides as NADP-Dependent Glyceraldehyde -3-Phosphate Dehydrogenase in paragraph 2. It is noted that the rabbits (i.e. the injected animals) were not challenged with group B streptococcus and the survival of such or resolution of infection or protection from infection were not established. No testing on the initial injected rabbits was performed. Instead, IgG specifically purified from the rabbits was injected into rat pups that were then challenged by an unknown route of infection. The route of infection, the type of antibody produced is critical to demonstrate efficacy of a vaccine. Declarant indicates that Table 1 shows that the survival rate for pups receiving "MS10" IgG is significant as compared to untreated (PBS control). However, Table 1 does not describe survival but "The number of rat pups sacrificed over time". If the pups are sacrificed then how is survival assessed ? Further, Declarant's protocol is completely different from the instantly claimed invention. The claims are drawn to active immunization and the declaration is drawn to passive immunization. Active immunization is stimulation of an individual's immune response in order to confer protection against disease whereas passive immunization is the use of antibody or primed lymphocytes from an immune individual to produce passive immunity against an antigen is substance or organism in a non-immune individual (Herbert et al, in The Dictionary of Immunology 4th edition, pages 20 and 125, Academic Press, 1995). In contrast to active immunization, passive immunization provides for administration of concentrated high levels of specific subsets of antibodies. There is no showing that the levels of IgG antibodies injected into the pups can be achieved by active immunization.

The declaration is devoid of any information in regard to the amount of purified IgG administered to the pups, such that any comparison with known IgG levels with other active vaccines producing IgG can be established. As such, the declaration is drawn to passive immunization with highly purified IgG administered in unknown amounts, where as the claims are specifically drawn to active immunization. There is no nexus provided in the declaration between the IgG levels required for passive immunization and those obtained by active immunization (i.e. the levels of IgG in the sera of the rabbits is not compared to the levels administered to the rat pups). The declaration does not address local infection or urinary tract infections as claimed. The declaration does not speak to the claimed invention, which is in fact drawn to active immunization. Finally, the declaration does not speak to fragments and the specification fails to teach a single fragment and identification and use of such is undue for reasons made of record. It is noted that enablement must be established in the specification at the time of filing and is to be commensurate in scope with the stated claims. *In re Hogan and Banks*, 194 USPQ 527 (1977). The art teaches that multiple distinct glyceraldehyde-3-phosphate dehydrogenases in cariogenic streptococci (Brown et al (Biochem. Biophys. Res. Commun. 43(1):217-24). Further, Kolberg et al (Infection and Immunity 64(9):3544-3547, 1996) teach that monoclonal antibodies that recognize a common penumonoccal protein with similarities to surface glyceraldehyde-3-phosphate dehydrogenase at the sequence level but demonstrated negligible cross-reaction with *S. pyogenes*. This clearly demonstrates that epitopes are not necessarily conserved cross-species, even within the same Genus of bacteria. As such, success with one particular protein can not predict success with any other given the lack of cross-reactivity and that multiple enzymes exist even within the same bacterium. Applicants have not shown that any bacterial glyceraldehyde -3-phosphate dehydrogenase obtained from different streptococcal species or different Genera of bacteria such as *Escherichia coli* are cross protective or prevent Group B Streptococcal infections. Such is the breath of that which is now claimed. Vaccine

fragments are not enabled for all the reasons made of record. Applicants argue that the skilled artisan can ascertain relevant fragments and test to see if they can be used as vaccine. This is not persuasive, discover, make and test to see if one could use is not the requisite standard under 112, first paragraph. Not a single active fragment for use is identified that is operable as a vaccine as claimed. There is no written description of any fragment that is useful. The argued skill in the art with respect to identifying epitopes, determining immunogenicity, determining vaccine potential is the essence of discovery and invention of vaccines. In applications directed to inventions in arts but where the results are unpredictable, the disclosure of a single species (i.e. the full length) usually does not provide an adequate basis to support generic claims (i.e. all fragments or all enzymes). *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. Applicants' have no written description for any desirable immunogenic fragments and the claimed fragments are not enabled for vaccines such and that applicants' are not entitled for dominance of further patentable inventions by claims that are insufficiently supported by the specification (*In re Fisher*, 166 USPQ 18, CCPA (1970)). Applicants' arguments rely upon the declaration, which is not persuasive for all the reasons set forth above.

New Rejections Based on Amendment

Claims 25, 27, 28, 32-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey

to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As to claims 25, 27, 28 and 32-44, the claims have been amended to recite "an isolated bacterial NADP-dependent glyceraldehyde-3-phosphate dehydrogenase". The specification does not provide written description basis for the now claimed genus. The specification teaches that SEQ ID NO:11 and the deduced amino acid sequence was homologous genes encoding a *Nonphosphorylating, NADP-Dependent Glyceraldehyde-3-Phosphate Dehydrogenase (NPGAP-3-DH) (page 10, lines 25-26*). The specification does not support conception for the now claimed broader genus of any "bacterial" NADP-Dependent Glyceraldehyde-3-Phosphate Dehydrogenase as claimed. The similar issue of broadening a genus to include species not contemplated by way of written description at the time of filing has been settled by the courts wherein claims of a reissue application were drawn to new matter since they broadly recite genus of "carrier particles" which is not disclosed in original patent, which discloses only subgenus of "magnetic carrier particles" and species of "iron, ferrites, nickel, and cobalt" carrier particles (*In re East and Harmon* (CCPA) 181 USPQ 716 (May 9, 1994)). Similarly, the instant specification discloses the subgenus of Nonphosphorylating, NADP-Dependent Glyceraldehyde-3-Phosphate Dehydrogenase (NPGAP-3-DH), but claims the broader genus of any bacterial NADP-Dependent Glyceraldehyde-3-Phosphate Dehydrogenase which necessarily includes those that do not meet the disclosed limitation of nonphosphorylating. There is no conception in this specification of vaccination with the claimed subgenus of *bacterial* enzymes per se. Additionally, the specification as filed does not set forth the genus of NADP-Dependent Glyceraldehyde-3-Phosphate Dehydrogenase proteins or the subgenus of bacterial enzymes. Applicants rely upon page 10 of the specification, but it describes the genus of nonphosphorylating NADP-Dependent Glyceraldehyde -3-Phosphate Dehydrogenase, one from a bacterium (*S. mutans*) and the others from plants. This does not provide conception for the now claimed subgenus of bacterial enzymes *per se*. The

subgenus of bacterial enzymes is not conceived of by way of written description at the time of filing.

The bacterial proteins for use are not described and claimed by way of structure and function. The structural features that establish the NADP-Dependent Glyceraldehyde-3-Phosphate Dehydrogenase as a bacterial or mammalian enzyme are not set forth in the claims. The specification was not in possession of the genus of bacterial enzymes suitable for active immunization. The specification does not teach a genus of suitable bacterial enzymes for vaccines and names only one from bacterium, *Streptoccus mutans*. The other enzymes are from plants. There is no description of the genus of bacterial enzymes either in the specification or the art. Applicants were not in possession of the invention, because the specification does not describe the genus of bacterial enzymes now claimed for use in vaccination. The specification fails to describe a single fragment or immunogenic fragment useful as claimed. There is no description of any fragment of any MS10 polypeptide, nor description of fragments that are "immunogenic". The specification either describes a fragment or it does not. In this case there are no fragments described. Reiteration of the words of the specification does not provide for adequate written description of a fragment of any particular sequence. The specification as filed does not describe any fragment of any protein that is therapeutic or immunogenic, and therefore Applicants were clearly not in possession of the claimed invention. Conception is more than a vague idea of how to solve a problem. The requisite means themselves and their interaction must also be comprehended. See *Mergenthaler v. Scudder* 1897 C.D. 724, 81 O.G. 1417 (D.C. Cir. 1897). There is no recognition of fragments, immunogenic fragments or vaccine fragments that can be specifically made and used as claimed.

Claims 45 and 46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicants argue that the specification teaches the now claimed method at page 2, lines 3-4, 11-16 and 27-30 and page 4, lines 11-15. Page 2, lines 3-4 broadly teaches "immunogens", lines 11-16 teach therapy with peptides or homologues, and lines 27-30 teach gene therapy for a therapeutic effect. None of these passages describe a method of making antibodies. The term "immunogen" is art defined as a substance that when introduced into the body stimulates humor or cell mediated immunity but not immunological tolerance (Herbert et al, in The Dictionary of Immunology 4th edition, page 90, Academic Press, 1995). As such, the broad concept of an immunogen does not lead to the specific species of a humoral response (i.e. the instantly claimed antibody) as opposed to a cell-mediated response. To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention and that the invention, in that context, is whatever is now claimed.. See MPEP 2163.02. Also, the failure to meet the written description requirement under 35 USC 112, first paragraph arises when the claims are changed after the filing date to change the scope of the disclosure, which does encompass setting forth subgeneric claims (see MPEP 2163.05). The subgenus as now claimed is a humoral response. Entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977). In order to satisfy the written description requirement, the blazemarks directing the skilled artisan to the claimed invention must be in the originally filed disclosure. It is not an issue whether one skilled in the art might be able to extrapolate the claimed invention from the teachings of the disclosure or whether the incorporated material would be obvious over what is expressly disclosed; but rather, it is a question whether the application as-filed necessarily discloses the claimed invention, a

method of making antibodies. Applicants argue that the claims are supported at page 4, lines 11-15. This passage indicates that the peptides can be used to elicit an immune response. An immune response is defined in the art as "the specific response to antigen. Thus includes the responses of cell-mediate immunity, humoral immunity and, in its widest sense immunological tolerance, though strictly speaking, the late is a state of specific immunological unresponsiveness." (Herbert et al, in The Dictionary of Immunology 4th edition, page 88, Academic Press, 1995). Therefore, this passage does not lead one skilled in the art to conception at the time of filing of the subgenus of a method of making an antibody as now claimed. Even if these passages were used in combination they still do not direct the skilled artisan to the claimed method and provide written description that Applicants had conceived to the now claimed method of making antibodies as part of the invention. It is noted that the definitions of immunogen and the definition of immune response are not equivalent and that Applicants are mixing different art defined concepts to attempt to arrive at a subgenus (humoral immunity) of a method that was not conceived in the specification as filed.

Status of Claims

All claims stand rejected.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 6:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patricia A. Duffy

Primary Examiner

Art Unit 1645